sum of the individual groups suggested in the Examiner's action. That is, there are cells covered by claim 1 which are not represented in any of the Examiner's proposed classes. Applicants submit that claim 1 is a linking claim for Groups I-X. Applicants respectfully remind the Examiner that, in accordance with MPEP 809, "should any linking claim be allowed, the restriction requirement must be withdrawn." Applicants suggest that the restriction requirement be withdrawn, and the provisional election instead be considered as an election of species for search purposes only.

Applicants also contend that the Examination of Groups I-X, as they are directed to cells containing a DNA encoding a receptor protein with a ligand binding domain and a DNA encoding an angiogenesis inhibitor and methods of using such cells, will involve searching of the same art and can therefore be examined together without any undue burden on the Examiner. In contrast, restriction adds significant costs to prosecution, and these costs impose a significant financial burden on small companies such as the assignee of the present invention.

Please enter the following amendments

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. (**Amended**) A cell containing

(a) a first genetic construct or pair of first genetic constructs encoding chimeric proteins comprising (i) at least one ligand-binding domain which can bind a selected ligand to form a ligand-crosslinked protein complex including the chimeric protein and (ii) a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains, and

(b) a target gene encoding an angiogenesis inhibitor under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain,

wherein transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.

2. **(Reiterated)** The cell of claim 1 wherein the chimeric proteins multimerize upon addition of ligand and wherein transcription of the target gene is responsive to the multimerization of the chimeric proteins.

3. **(Reiterated)** The cell of claim 1 wherein the ligand binding domain is selected from the group consisting of an immunophilin domain, a cyclophilin domain, a steroid hormone binding domain and an antibiotic binding domain.

4. **(Amended)** The cell of claim 1 wherein the angiogenesis inhibitor is selected from the group consisting of thrombospondin, angiostatin, endostatin, angiostatin-endostatin fusion proteins, angiiopoietin-2, a soluble receptor for VEGF, a dominant negative form of VEGF, anti-VEGF antibodies, soluble Tie2/Tek receptor and a 16 kD fragment of prolactin.

5. **(Reiterated)** The engineered cell of claim 1 or 4 in which the target gene encodes a peptide sequence of human origin.

14. **(Amended)** A method for rendering a cell capable of regulatable expression of a target gene following exposure of said cell to a selected ligand, which method comprises introducing into said cell:

(a) a first genetic construct or pair of first genetic constructs encoding chimeric proteins comprising (i) at least one ligand-binding domain which can bind a selected ligand to form a ligand-corsslinked complex including the chimeric protein and (ii) a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains, and

(b) a target gene under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain,

wherein the target gene encodes an angiogenesis inhibitor or a tumor specific antigen, and wherein the transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.

15. (**Amended**) The method of claim 14 wherein the angiogenesis inhibitor is selected from the group consisting of thrombospondin, angiostatin, endostatin, angiostatin-endostatin fusion proteins, angiopoietin-2, a soluble receptor for VEGF, a dominant negative form of VEGF, anti-VEGF antibodies, soluble Tie2/Tek receptor and a 16 kD fragment of prolactin.

17. (**Amended**) The method of claim 14 or 16 wherein the genetic constructs are introduced into a cell maintained in vitro.

18. (**Amended**) The method of claim 14 or 16 wherein the genetic constructs are introduced into a cell present within a host organism.

19. (**Reiterated**) The method of claim 14 wherein the chimeric proteins multimerize upon addition of ligand and wherein transcription of the target gene is responsive to the multimerization of the chimeric proteins.

20. (**Reiterated**) The method of claim 14 or 16 wherein the ligand binding domain is selected from the group consisting of an immunophilin domain, a cyclophilin domain, a steroid hormone binding domain and an antibiotic binding domain.

Please enter the following new claims:

24. (New) The method of claim 14, wherein at least one of (a) or (b) is introduced into said cell by a viral vector.

25. (New) The method of claim 24, wherein the viral vector is selected from the group consisting of adenovirus, adeno-associated virus, herpesvirus, and retrovirus.

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26. (New) The method of claim 14, wherein the cell is a mammalian cell.

27. (New) The method of claim 26, wherein the mammalian cell is a human cell.

28. (New) The method of claim 14, wherein the cell is a cell type selected from the group consisting of neural, mesenchymal, cutaneous, mucosal, stromal, spleen, reticuloendothelial, epithelial, endothelial, kidney, gastrointestinal and pulmonary cells.

29. (New) The method of claim 14, wherein the genetic construct further comprises one or more selectable markers.

30. (New) The method of claim 29, wherein the selectable marker is selected from the group consisting of an antibiotic resistance gene and herpes simplex virus-thymidine kinase.

31. (New) The method of claim 14, wherein the target gene is a human gene.

32. (New) The method of claim 14, wherein the selected ligand binds the ligand-binding domain with a K_d value less than 10^{-6} M.

33. (New) The method of claim 14, wherein the selected ligand binds the ligand-binding domain with a K_d value less than 10^{-9} M.

34. (New) The method of claim 14, wherein the selected ligand is not a protein and wherein the selected ligand has a molecular weight less than 5 kDa.

35. (**New**) The method of claim 14, wherein the chimeric protein includes two or more ligand-binding domains having different ligand binding specificities.

36. (**New**) The method of claim 14, wherein at least one of the ligand-binding domains is from 50 to 350 amino acid residues in length.

37. (**New**) The method of claim 14, wherein said selected ligand is membrane permeable.

38. (**New**) The method of claim 14, wherein said selected ligand is orally active.

The amended claims are restated below to reflect changes with respect to the last filing.

1. (**Amended**) A cell containing

   (a) a first ~~DNA~~ genetic construct or pair of first ~~DNA~~ genetic constructs encoding chimeric proteins ~~protein~~ comprising (i) at least one ~~receptor~~ ligand-binding domain which can bind ~~capable of binding to~~ a selected ligand to form a ligand-crosslinked protein complex including the chimeric protein and (ii) ~~another~~ a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains ~~the receptor domain~~, and

   (b) a target gene encoding an angiogenesis inhibitor under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain,

   wherein transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.

4. (**Amended**) The cell of claim 1 wherein the angiogenesis inhibitor is selected from the group consisting of thrombospondin ~~thrombosponding~~, angiostatin, endostatin,

angiostatin-endostatin fusion proteins, angiiopoietin-2, a soluble receptor for VEGF, a dominant negative form of VEGF, anti-VEGF antibodies, soluble Tie2/Tek receptor and ~~the~~ a 16 kD fragment of prolactin.

14. (**Amended**) A method for rendering a cell ~~cells~~ capable of regulatable expression of a target gene following exposure of said cell ~~the cells~~ to a selected ligand, which method comprises introducing into said cell ~~the cells~~:

(a) a first ~~DNA~~ genetic construct or pair of first ~~DNA~~ genetic constructs encoding chimeric proteins comprising (i) at least one ~~receptor~~ ligand-binding domain which can bind ~~capable of binding to~~ a selected ligand to form a ligand-corsslinked complex including the chimeric protein and (ii) ~~another~~ a second protein domain, which is heterologous with respect to at least one of the ligand-binding domains ~~the receptor domain~~, and

(b) a target gene under the expression control of a transcriptional control element responsive to binding of ligand to the ligand binding domain,

wherein the target gene encodes an angiogenesis inhibitor or a tumor specific antigen, and wherein the transcription of the target gene is regulated in a manner dependent on the expression of the chimeric protein and the presence of the ligand.

15. (**Amended**) The method of claim 14 wherein the angiogenesis inhibitor is selected from the group consisting of thrombospondin, angiostatin, endostatin, angiostatin-endostatin fusion proteins, angiopoietin-2, a soluble receptor for VEGF, a dominant negative form of VEGF, anti-VEGF antibodies, soluble Tie2/Tek receptor and ~~the~~ a 16 kD fragment of prolactin.

17. (**Amended**) The method of claim 14 or 16 wherein the ~~DNA~~ genetic constructs are introduced into a cell ~~cells~~ maintained in vitro.